Remarks

The Office Action mailed February 7, 2006, has been received and reviewed. Claims 16 and 17 having been added, the pending claims are claims 1-9 and 13-17. Reconsideration and withdrawal of the rejections are respectfully requested. Support for new claims 16 and 17 is found throughout the specification. For example, support for new claim 16 is found in original claim 1 and support for new claim 17 is found in original claim 13.

Claims 13-15

The Office Action mailed February 7, 2006 (see item 6, page 1), includes claims 13-15 in the statement of rejection. However, a review of the Office Action indicates that claims 13-15 are not included in any of the rejections statements included within the Office Action. Thus, Applicants submit that the status of claims 13-15 remains "allowed," as indicated in the Notice of Allowance mailed September 21, 2005. The Examiner is requested to correct the record to reflect the allowance of claims 13-15.

The 35 U.S.C. §102 Rejection

The Examiner rejected claims 1-6 under 35 U.S.C. §102(e) as being anticipated by Madonna et al. (U.S. 2004/0224359). This rejection is respectfully traversed.

Claims 1-6 are drawn to a method comprising:

> "contacting the sample with bacteriophage comprising a binding agent . . . ;
>
> incubating the sample under conditions effective for the bacteriophage comprising a binding agent to infect the bacterial cell . . .;
>
> contacting the sample with a substrate comprising immobilized ligand for the binding agent . . .;
>
> removing the complexes of bacteriophage comprising a binding agent and substrate comprising immobilized ligand from the sample; and
>
> detecting new bacteriophage in the sample from which complexes have been removed. . . ."

The present application (filed October 15, 2003) claims priority to U.S. Provisional Application 60/418,822 (filed October 15, 2002). The Examiner asserted that the teachings of U.S. Provisional Application 60/418,822 do not provide support for the presently claimed invention, and thus, Madonna et al. (U.S. 2004/0224359, filed April 10, 2003) anticipates claims 1-6 under 35 U.S.C. §102(e). Specifically, the Examiner asserted that U.S. Provisional Application 60/418,822 does not provide support for the presently claimed method, a method that "involves the introduction to a sample of a phage comprising a binding agent, wherein the phage is not attached to a probe or other support. . . [and] a probe comprising a ligand to the binding agent is used to remove the phage with a binding agent from the sample after an incubation step in which progeny phage may be produced (if the target bacterium is in the sample)" (pages 3-4, Office Action mailed February 7, 2006).

Applicants adamantly, yet respectfully, disagree and submit that U.S. Provisional Application 60/418,822 provides support for the presently claimed invention. Specifically, Applicants direct the Examiner's attention to Example 3 ("Detection and quantification of *Bacillus subtilis* by the use of the bacteriophage ø29") of U.S. Provisional Application 60/418,822 (see page 18, line 24 to page 19, line 19). Example 3 describes a method of detecting a bacterial cell in a sample comprising:

> "[b]acteriophage ø29 of *Bacillus subtilis* . . . is grown, purified and biotinylated . . . such that the phage retains infectivity . . . . Free biotinylated phage particles are added to the sample containing *B. subtilis* and nutrients needed for cell growth, and the sample is incubated at 37°C with gentle agitation. All target cells are infected, and at 10 minutes excess biotinylated input phages are removed by the use of streptavidin-coated magnetic beads and a magnet. . . . After lysis of the infected cells . . . the 1,000 progeny particles produced per cell are retrieved by the addition of new magnetic beads coated with anti-ø29 antibodies and the use of a magnet. These bead-phage complexes are . . . stained with Alexa dye, washed to remove free dye, and observed directly by light microscopy at a magnification of 2,000 . . . . The number of phage produced reflects the number of target bacteria in the sample."

Applicants respectfully submit that Example 3 discloses a method of detecting a bacterial cell in a sample that is the same as the claimed method; a method "comprising: contacting the sample with bacteriophage comprising a binding agent . . . ; incubating the sample under conditions effective for the bacteriophage comprising a binding agent to infect the bacterial cell . . .; contacting the sample with a substrate comprising immobilized ligand for the binding agent . . .; removing the complexes of bacteriophage comprising a binding agent and substrate comprising immobilized ligand from the sample; and detecting new bacteriophage in the sample from which complexes have been removed." Applicants submit that U.S. Provisional Application 60/418,822 provides support for the presently claimed invention. Reconsideration and withdrawal of the rejection of claims 1-6 under 35 U.S.C. §102(e) as being anticipated by Madonna et al. (U.S. 2004/0224359) is requested.

Further, Applicants submit that Madonna et al. does not teach a method that is the same as the claimed method. Madonna et al. teach a method in which "immunomagnetic separation (IMS) is used to separate target bacterium that may be in a liquid mixture from other constituents in the mixture. A low concentration of a bacteriophage *is subsequently used to infect target bacterial cells that have been captured using the IMS technique*" (see abstract, see, also, Figures 1-3 and page 4, paragraphs [0037-0039] (emphasis added)). The method of Madonna et al. involves first isolating bacterium from the sample by the use of immunomagnetic separation prior to contacting the sample with a bacteriophage (see page 5, paragraphs [0041-0052]). Thus, the method taught by Madonna et al. is not the same as the method of claims 1-6 and Madonna et al. does not anticipate the methods of claims 1-6. Reconsideration and withdrawal of the rejection of claims 1-6 under 35 U.S.C. §102(e) as being anticipated by Madonna et al. (U.S. 2004/0224359) is requested.

Applicants acknowledge the Examiner's statement that although Madonna et al. claims priority to an earlier provisional application, the provisional application does not disclose the presently claimed invention (see top of page 5, Office Action mailed February 7, 2006).

The 35 U.S.C. §103 Rejections

Madonna et al. further in view of Terlesky et al., Stroobant et al., and Petersen et al.

The Examiner rejected claims 6 and 9 under 35 U.S.C. §103(a) as being unpatentable over Madonna et al. as applied to claims 1-6 and further in view of the teachings of Terlesky et al. (U.S. 2004/0152085), Stroobant et al. (U.S. 2002/0090637), and Petersen et al. (U.S. 2002/00042125). This rejection is respectfully traversed.

As discussed above, the present application (filed October 15, 2003) claims priority to U.S. Provisional Application 60/418,822 (filed October 15, 2002). Thus, Applicants submit that Terlesky et al. (U.S. 2004/0152085), which was filed on February 4, 2003, and published on August 5, 2004, does not qualify as prior art under 35 U.S.C. §102(e) and cannot be used in a rejection under 35 U.S.C. §103(a).

As discussed above, Applicants submit that Madonna et al. does not teach a method that is the same as the method of claims 1-6. Further, Applicants submit that the teachings of Terlesky et al., Stroobant et al., or Petersen et al. do not correct this deficiency in the teachings of Madonna et al. Thus, Madonna et al. as applied to claims 1-6 and further in view of the teachings of Terlesky et al., Stroobant et al., and Petersen et al. does not "render claims 6 and 9 obvious," as asserted by the Examiner. Reconsideration and withdrawal of this rejection of claims 6 and 9 under 35 U.S.C. §103(a) is requested.

One of the critical, basic elements necessary to establish a *prima facie* case of nonobviousness of the claimed invention is that "there must be a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings" ((MPEP § 2143). Applicants submit that this requisite motivation to combine the teachings of Madonna et al. with any of Terlesky et al., Stroobant et al., or Petersen et al. is absent. Madonna et al. teaches methods for detecting low concentrations of bacteria in a liquid solution (see abstract). Terlesky et al. teaches "a substrate for collecting nucleic acids . . . comprising a surface; an aerogel coated on said surface; an active silane attached to said aerogel; and a nucleic acid binding agent attached to said silane" (see abstract). Stroobant et al. teaches "methods for identifying, isolating and comparing proteins and other biomolecules differing between two complex biological samples using affinity chromatography and phage display techniques" (see abstract). Petersen et al. teaches "a cartridge for performing various operations on a fluid sample as the fluid flows through a series of interconnected, interactive regions within the cartridge" (see page 3, paragraph [0042]). Applicants submit that one of ordinary skill in the art would not be motivated to combine the teachings of Madonna et al. with the teachings of Terlesky et al., Stroobant et al., or Petersen et al. to obtain the present invention. Reconsideration and withdrawal of this rejection of claims 6 and 9 under 35 U.S.C. §103(a) is requested.

Madonna et al. further in view of Teodorescue et al.

The Examiner rejected claims 7 and 8 under 35 U.S.C. §103(a) as being unpatentable over Madonna et al., as applied to claims 1-6, and further in view of Teodorescue et al. (U.S. Patent No. 4,797,363). This rejection is respectfully traversed.

As discussed above, Applicants submit that Madonna et al. does not teach a method that is the same as the method of claims 1-6. Further, Applicants submit that the teachings of Teodorescue et al. do not correct this deficiency in the teachings of Madonna et al. Thus, Madonna et al. as applied to claims 1-6 and further in view of the teachings of Teodorescue et al. does not render claims 7 and 8 obvious, as asserted by the Examiner. Reconsideration and withdrawal of this rejection of claims 7 and 8 under 35 U.S.C. §103(a) is requested.

Further, Applicants submit that this requisite motivation to combine the teachings of Madonna et al. with Teodorescue et al. is absent. Madonna et al. teach methods for detecting low concentrations of bacteria in a liquid solution, wherein a low concentration of bacteriophage are used to infect the bacteria (see abstract). Teodorescue et al. teach methods "for the identification and quantification of molecular and cellular materials . . . wherein bacteriophage are used, in a manner similar to antibodies, as "visualizers" to bind to the molecular or cellular materials (see abstract; col. 2, lines 58-68; and col. 3, lines 43-45). Applicants submit that one of ordinary skill in the art would not be motivated to combine the very different methods taught by Madonna et al. and Teodorescue et al. to obtain the present invention. Reconsideration and withdrawal of this rejection of claims 7 and 8 under 35 U.S.C. §103(a) is requested.

Madonna et al. further in view of Olsvik et al. and Yazdankhah et al.

The Examiner rejected claims 7 and 8 under 35 U.S.C. §103(a) as being unpatentable over Madonna et al. as applied to claims 1-6 above, and further in view of the teachings of Olsvik et al. (Clin Micro. Rev., 7:43-54) and Yazdankhah et al. (Vet. Micro., 62:17-26). This rejection is respectfully traversed.

The Examiner asserted that claims 7 and 8 are drawn to a method "wherein the new bacteriophage are detected by complexing the new phage with a substrate comprising an immobilized binding agent to the new phage, and detecting the phage/substrate complex" (page 7, Office Action mailed February 7, 2006). Applicants respectfully disagree and submit that claims 7 and 8 contain no recitations directed at "wherein the new bacteriophage are detected by complexing the new phage with a substrate comprising an immobilized binding agent to the new phage, and detecting the phage/substrate complex," as asserted by the Examiner. Reconsideration and withdrawal of this rejection of claims 7 and 8 under 35 U.S.C. §103(a) is requested.

As previously discussed, Applicants submit that Madonna et al. does not teach a method that is the same as the method of claims 1-6. Further, the teachings of Olsvik et al. and Yazdankhah et al. do not correct this deficiency in the teachings of Madonna et al. Thus, Madonna et al. as applied to claims 1-6 and further in view of Olsvik et al. and Yazdankhah et al. does not render claims 7 and 8 obvious, as asserted by the Examiner. Reconsideration and withdrawal of this rejection of claims 7 and 8 under 35 U.S.C. §103(a) is requested.

Further, Applicants submit that the requisite motivation to combine the teachings of Madonna et al. with Olsvik et al. and Yazdankhah et al. is absent. Madonna et al. teach methods for detecting low concentrations of bacteria in a liquid solution, wherein immunomagnetic separation is used to separate target bacterium from other constituents in the mixture, wherein a low concentration of a bacteriophage for the target bacterium is subsequently used to infect target bacteria, and wherein Matrix assisted laser desorption ionization/time-of-flight-mass spectroscopy (MALDI/TOF-MS) is used to determine if proteins associated with a bacteriophage are present (see abstract). As Applicants have previously presented (see page 8 of the Amendment and Response filed March 16, 2005), Olsvik et al. teach magnetic separation techniques for use in diagnostic microbiology. The very limited teachings of Olsvik et al. relating to the detection of bacteriophage (referred to therein as "viruses") are limited to the use of oligonucleotide probes linked to magnetic beads to be used as primers in a polymerase chain reaction (PCR) for the direct detection of viral RNA or DNA in a sample (see Oslvik et al. pages 50-51). Applicants disagree with the Examiner's assertion that "Olsvik teaches a method for the detection and identification of viruses . . . comprising their capture on a substrate with a ligand or binding agent thereto" (page 7 of Office Action mailed February 7, 2006) and submit that the Examiner's assertion is a mischaracterization of the teachings of Oslvik et al. As Applicants have previously presented (see page 14 of the Amendment and Response filed March 16, 2005), Yazdankhah et al. teach a method of detecting *Staphylococcus* bacteria in milk samples by the use of magnetic beads coated with monoclonal antibodies specific to the *Staphylococcus* bacteria. Applicants submit that one of ordinary skill in the art would not be motivated to combine the disparate teachings of Madonna et al. with Olsvik et al. and Yazdankhah et al. to obtain the method of claims 7 and 8.

The Examiner asserted "it would have been obvious to those of skill in the art that the bead/antibody binding agent could also be adapted to detect phage. As the use of such beads for the detection of phage was known in the art, and would have been recognized as an alternative to the plague assay for the detection of the new phage, it would have been obvious to those in the art to substitute such a method for the detection of the new phage for the mass spectrometry assay used in the method of Madonna" (see page 7, Office Action mailed February 7, 2006). Applicants respectfully disagree and request that the Examiner support his assertions of what was known in the art be supported by the citation of the prior art documents that provide such teachings.

In view of the above discussion, Applicants submit that one of ordinary skill in the art would not be motivated to combine the very different methods taught by Madonna et al., Olsvik et al., and Yazdankhah et al. et al. to obtain the present invention. Reconsideration and withdrawal of this rejection of claims 7 and 8 under 35 U.S.C. §103(a) is requested.

Summary

It is respectfully submitted that the pending claims 1-9 and 13-17 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives at the telephone number listed below if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
By
Mueting, Raasch & Gebhardt, P.A.
P.O. Box 581415
Minneapolis, MN 55458-1415
Phone: (612) 305-1220
Facsimile: (612) 305-1228
Customer Number 26813

May 8, 2006
Date

By: Nancy A. Johnson
Nancy A. Johnson
Reg. No. 47,266
Direct Dial (612)305-4723

NAJ/skd

CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to, Commissioner for Patents, Mail Stop Amendment, P.O. Box 1450, Alexandria, VA 22313-1450, on this 8th day of May, 2006, at 9:45 a.m. (Central Time).

By: Sue Dombroske
Name: Sue Dombroske